II. REMARKS

Formal Matters

Claims 15, 18, 21 and 68 are pending after entry of the amendments set forth herein.

Claims 15, 17, 18, 21 and 66 were examined and were rejected.

Claim 15 is amended. The amendments to claim 15 were made solely in the interest of expediting prosecution, and are not to be construed as acquiescence to any objection or rejection of any claim. Support for the amendments to claim 15 is found in the claims as originally filed, and throughout the specification, in particular at the following exemplary locations: pg. 41, line 10 – pg. 42, line 27. Accordingly, no new matter is added by these amendments.

Claims 17 and 66 are canceled without prejudice to renewal, without intent to acquiesce to any rejection, and without intent to surrender any subject matter encompassed by the canceled claims. Applicants expressly reserve the right to pursue any canceled subject matter in one or more continuation and/or divisional applications.

Claim 68 is added. Support for new claim 68 is found in the claims as originally filed, and throughout the specification, including the following exemplary locations: pg. 41, line 10 – pg. 42, line 27. Accordingly, no new matter is added by new claim 68.

Applicants respectfully request reconsideration of the application in view of the remarks made herein.

Specification

The Office Action indicated acknowledgement of Applicants' statement made in the Amendment dated October 10, 2006, that SEQ ID NO: 10 is a mouse amino acid sequence as noted in the sequence listing. However, the Office Action also stated that "[a]ppropriate correction or clarification is required."

Applicants submit that the appropriate correction or clarification has been made. The Examiner is thus respectfully requested to withdraw the rejection. If the Examiner is requesting additional correction or clarification, Applicants request that the Examiner clarify the nature of the additional correction or clarification requested.

Claim Objections

Claim 17 was objected to. The Office Action stated that claim 17 is objected to because it is the same as claim 15 from which it depends.

Claim 17 has been cancelled; therefore, this objection to claim 17 is moot.

Rejection under 35 U.S.C. 102(e)

Claims 15, 17, 18, 21 and 66 were rejected as allegedly anticipated by Sturley et al. (U.S. Patent Number 6,100,077) ("Sturley"). Applicants respectfully traverse the rejection.

Claims 17 and 66 are cancelled without prejudice to renewal; therefore, the rejection as applied to claims 17 and 66 is moot.

A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference. *Verdegaal Bros. v. Union Oil of California*, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987).

Independent claim 15 has been amended as follows:

> An *in vitro* screening assay for determining a candidate agent's diacylglycerol-*O*-acyltransferase (DGAT) inhibitory activity, said assay comprising:
>
> (a) contacting a DGAT polypeptide with said candidate agent, wherein said DGAT polypeptide exhibits diacylglycerol-*O*-acyltransferase activity, and wherein said DGAT polypeptide comprises an amino acid sequence having at least 98% amino acid sequence identity to the amino acid sequence set forth in SEQ ID NO:6; and
>
> (b) detecting a change in DGAT enzymatic activity of said DGAT polypeptide compared to a control to determine said candidate agent's DGAT inhibitory activity, wherein said detecting comprises detecting incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor.

Applicants submit that Sturley fails to teach each and every element as set forth in claim 15 as currently amended. Specifically, Sturley fails to teach "detecting a change in DGAT enzymatic activity of said DGAT polypeptide compared to a control to determine said candidate agent's DGAT inhibitory activity, wherein said detecting comprises detecting incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor."

The Office Action asserts that Sturley discloses an assay which measures the incorporation of [14C]-oleate into sterol ester in the presence of a DGAT polypeptide having the sequence disclosed in SEQ ID NO: 6 of the instant application. However, this does not amount to a disclosure of detecting

incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor. The incorporation of [14C]-oleate into sterol ester demonstrates ACAT activity while the incorporation of a detectably labeled fatty acyl CoA into a diacylglycerol acceptor is an assay of DGAT activity. The Sturley patent provides the following discussion of the assay performed.

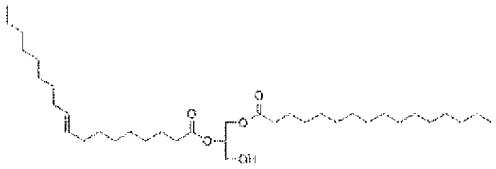
> "Assay of ACAT activity in ACAT negative yeast transformed with ARGP1 and ARGP2. The ability of ARGP1 and ARGP2 to esterify sterols was assayed in a sterol esterification deficient yeast strain (SCY059) in which the endogenous ARE genes were deleted. **Microsomes from these yeast, transformed with an expression vector harboring no insert or cDNA inserts for ARGP1, ARGP2, or human ACAT1 were assayed in vitro for the incorporation of [^{14}C]-oleate into sterol ester.** Since we previously demonstrated that cholesterol is the preferred substrate for mammalian ACAT enzymes (27, 32), assays were performed with exogenous cholesterol supplied in Triton WR-1339. As shown in Table 1, ARGP2 forms cholesterol ester at a rate of 49 pmol/minute/μg microsomal protein. This is 24-fold over background and about 15% of the activity detected in microsomes from ACAT1 transformants. We therefore renamed ARGP2 as ACAT2. **ARGP1 did not display significant ACAT activity.**" (Column 20, lines 17-34; emphasis added)

This experimental section makes it clear that the described assay measures ACAT and not DGAT activity. At most, the described assay shows that ARGP1 (described by Sturley as a DGAT) does not show activity in incorporating [^{14}C]-oleate into sterol ester, i.e., ARGP1 did not display significant **ACAT** activity. This assay does not describe detecting a change in DGAT enzymatic activity since, as stated by Sturley, ARGP1 does not show significant activity in the described assay.

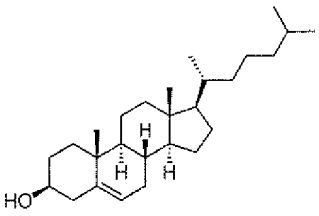
In contrast to the above, the present application discloses operative DGAT activity assays in which the incorporation of [^{14}C]oleoyl-CoA into a diacylglycerol acceptor is measured in the presence of a DGAT enzyme (Specification, pg. 41, line 10 – pg. 42, line 27).

As discussed above, the Office Action indicates that Sturley discloses the incorporation of [14C]-oleate into **sterol ester**. Sturley also indicates that since cholesterol is the preferred substrate for mammalian ACAT enzymes, the assays were performed with exogenous cholesterol supplied. Finally, Sturley indicates that the formation of cholesterol ester was subsequently monitored. Cholesterol is not a diacylglycerol acceptor. It is clear from a quick review of the chemical formulas for cholesterol and diacylglycerol (see structures below) that these two molecules represent significantly different chemical substrates. As such, Sturley, which discusses the use of cholesterol as a substrate for the formation of

cholesterol ester, does not disclose or suggest an assay which utilizes a diacylglycerol as a substrate.



Exemplary diacylglycerol molecule



Cholesterol molecule

Conclusion as to the rejection under 35 U.S.C.§102(e)

Applicants submit that the rejection of claims 15, 17 and 66 under 35 U.S.C. § 102(e) has been adequately addressed in view of the remarks set forth above. Since rejected claims 18 and 21 each depend from amended claim 15, the above remarks apply equally to the rejection of those claims. The Examiner is thus respectfully requested to withdraw the rejection.

III. CONCLUSION

Applicants submit that all of the claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-0815, order number UCAL-105CIP2.

Respectfully submitted,
BOZICEVIC, FIELD & FRANCIS LLP

Date: July 3, 2007

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